



Technical Support Document: Toxicology Clandestine Drug Labs/ Methamphetamine

Volume 1, Number 13

EPHEDRINE and PSEUDOEPHEDRINE

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Introduction

The clandestine synthesis of methamphetamine (meth) and other illegal drugs is a growing public health and environmental concern. For every pound of meth synthesized there are six or more pounds of hazardous materials or chemicals produced. These are often left on the premises, dumped down local septic systems, or illegally dumped in backyards, open spaces, in ditches along roadways or down municipal sewer systems. In addition to concerns for peace officer safety and health, there is increasing concern about potential health impacts on the public and on unknowing inhabitants, including children and the elderly, who subsequently occupy dwellings where illegal drug labs have been located.

The Office of Environmental Health Hazard Assessment (OEHHA), in cooperation with the Department of Toxic Substances Control (DTSC), has been charged with assisting in identifying and characterizing chemicals used or produced in the illegal manufacturing of methamphetamine, which pose the greatest potential human health concerns. To address in part this growing environmental problem and the need for public health and safety professionals to make appropriate risk management decisions for the remediation of former methamphetamine laboratory sites, OEHHA has developed two types of chemical-specific information documents.

The first set, technical support documents (TSDs), are referenced, multi-page publications, which contain important health and safety data, exposure limits, and key information for recognizing chemicals used or produced during the manufacturing of methamphetamine. These documents will likely be most helpful to health and safety officers, industrial hygienists, or others interested in more detailed toxicological information. The second set, two-page fact sheets, contain much of the same information as the corresponding TSDs; however, the details are presented in a more succinct, graphical format. The fact sheets will be helpful to individuals, including the public, who want to be able to quickly recognize potential chemicals of concern found in illegal methamphetamine labs in order to avoid inadvertent exposures and resulting health impacts.

For more information or to obtain copies of these and other documents, contact:

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I. Chemical Name

A. EPHEDRINE & PSEUDOEPHEDRINE (C₁₀H₁₅NO)

NOTE: This Technical Support Document summarizes information on the health hazards of ephedrine and pseudoephedrine. Where information pertains solely to one drug, it is so noted. Ephedrine and pseudoephedrine are stereoisomers, i.e., they have the same molecular formula (C₁₀H₁₅NO) and the same sequence of bonds, but different three dimensional spatial arrangements. At the molecular level, ephedrine and pseudoephedrine each consist of a pair of non-super imposable mirror images, which are called *d*- and *l*- enantiomers. Each enantiomer has slightly different pharmacological potency and biological effects. Pharmaceutical formulations of ephedrine and pseudoephedrine may contain only the *d*- enantiomer, only the *l*- enantiomer, or a mixture of the *d*- and *l*- enantiomers.

B. Synonyms

Ephedrine: α -[1-(methylamino) ethyl]benzene-methanol, α -[1-(methylamino)ethyl]benzyl alcohol, 2-methylamino-1-phenyl-1-propanol, 1-phenyl-1-hydroxy-2-methylaminopropane, 1-phenyl-2-methylaminopropanol, α -hydroxy- β -methylaminopropylbenzene, Ma Huang.

dl-Ephedrine: racemic ephedrine, racephedrine.

dl-Ephedrine hydrochloride: racephedrine hydrochloride, Ephetonin, Ephedral, Sanedrine.

dl-Ephedrine sulfate: racephedrine sulfate.

l-Ephedrine: l-erythro-2-(methylamino)-1-phenylpropan-1-ol.

dl-Pseudoephedrine: dl-threo-2-(methylamino)-1-phenyl-propan-1-ol.

d-Pseudoephedrine: d-isoephedrine.

d-Pseudoephedrine hydrochloride: Galpseud, Novafed, Rhinalair, Otrinol, Sinufed, Sudafed.

d-Pseudoephedrine sulfate: Afrinol (Merck, 1996).

II. Role in Clandestine Drug Synthesis: Methamphetamine

Ephedrine and pseudoephedrine are precursors in the synthesis of methamphetamine (Turkington, 2000).

III. Chemical Description

A. Appearance

Ephedrine appears as a waxy solid or as white to colorless granules, powder, or crystals (HSDB, 2002A; Turkington, 2000). Pseudoephedrine is a white powder (Acros, 2000B). The powders may become yellow upon standing (Turkington, 2000).

For pharmaceutical uses, Ephedrine and pseudoephedrine are often marketed as white, red, or blue tablets (e.g., Sudafed®). In clandestine methamphetamine labs, the tablets may be ground up and partially dissolved in water or alcohol. The resulting sludge is filtered using coffee filters or any makeshift filtering device such as a mop bucket wringer. In clandestine laboratories that are engaged in large scale production of methamphetamine, ephedrine and pseudoephedrine may be contained in fiberboard shipping drums.

B. Taste

Bitter.

C. Odor

None; however, ephedrine and pseudoephedrine may smell musty upon standing (Turkington, 2000).

D. Odor Threshold

Not applicable.

E. Irritancy Threshold

Not available.

F. Odor Safety Class

Not applicable.

G. Vapor Pressure and Density

Ephedrine and pseudoephedrine are solids at room temperature and are not volatile.

IV. Containers and Packaging

A. Commercial Products

Ephedrine and pseudoephedrine are sold over-the-counter in tablet or liquid form. See section II, B.

B. Pharmaceutical Use

Ephedrine has been used as a bronchodilator, nasal decongestant, mydriatic (pupil dilator), and a central nervous system stimulant. It has also been used to counteract hypotension associated with anesthesia and in the treatment of enuresis (urinary incontinence) and myasthenia gravis (a neurodegenerative disease involving voluntary muscles) (USP, 1998; Merck, 1996). Ephedrine occurs naturally in Ma Huang, which is in herbal medicines and supplements (Merck, 1996).

Pseudoephedrine is used to relieve the symptoms of nasal, sinus, and eustachian tube congestion due to the common cold, hay fever, or other respiratory allergies (USP, 1998; PDR, 2002). Pseudoephedrine is also used with other medications in the treatment of allergic rhinitis, croup, sinusitis, acute otitis media and acute tracheobronchitis (USP, 1998).

V. Chemical Hazards

A. Reactivity

Ephedrine and pseudoephedrine are stable under normal temperatures and pressures (Acros, 2000A; Acros, 2000B).

B. Flammability

Dusts of *l*-ephedrine hydrochloride at sufficient concentrations can form explosive mixtures with air (Acros, 2000A). Hazardous decomposition products include nitrogen oxides, carbon monoxide, carbon dioxide, nitrogen, and hydrogen chloride gas (for the hydrochloride forms) (Acros, 2000A; Sigma, 1997; Sigma, 2002A; Sigma, 2002B).

C. Chemical Incompatibilities

Ephedrine and pseudoephedrine are incompatible with strong oxidants (Acros, 2000A; Sigma, 2002B).

VI. Health Hazards

A. General

Ephedrine is a central nervous system stimulant that may produce nervousness, anxiety, apprehension, fear, tension, agitation, excitation, restlessness, weakness, irritability, talkativeness, or insomnia (HSDB, 2002A). Large doses of ephedrine may result in dizziness, lightheadedness, tremor, hyperactive reflexes, hypertension (high blood pressure), and vertigo (HSDB, 2002A; PDRHM, 1998). Large parenteral (routes other than oral) doses of ephedrine may cause confusion, delirium, hallucinations, or euphoria. In addition, paranoid psychoses and visual auditory hallucinations may occur at extremely high doses. Ephedrine may also cause the following: throbbing headache; respiratory difficulty; fever or a feeling of warmth; paleness; dryness of the nose and throat; chest pain; sweating; mild abdominal discomfort; vomiting; palpitation; tachycardia (rapid heartbeat); potentially fatal arrhythmias (alteration in heartbeat), including ventricular fibrillation; acute urinary retention or difficulty in urination; hypertension (high blood pressure), which may result in intracranial hemorrhage; nausea; and loss of appetite (HSDB, 2002A). Ephedrine has been known to cause allergic sensitization. *l*-Ephedrine hydrochloride may have a local anesthetic effect on exposed skin (Lewis, 2002). *l*-Ephedrine hydrochloride may cause skin, eye, mucous membrane, upper respiratory tract, and digestive tract irritation (Acros, 2000C; Sigma, 1997).

Symptoms of toxicity associated with pseudoephedrine include convulsions, hallucinations, irregular or slow heartbeat, shortness of breath, trouble breathing, an increase in blood pressure, nervousness, restlessness, excitement, trouble sleeping, difficult or painful urination, dizziness, lightheadedness, drowsiness, fast or pounding heartbeat, increased sweating, nausea, vomiting, trembling, unusual paleness, or weakness (USP, 1998; HSDB, 2002B). *d*-Pseudoephedrine hydrochloride exposure may cause eye, skin, and digestive tract irritation, as well as neurological and central nervous system effects (Acros, 2000B).

B. Acute Effects

Symptoms of high dose, acute ephedrine exposure include severe outbreaks of sweating, enlarged pupils, spasms, and elevated body temperature, with heart failure and asphyxiation leading to death (PDRHM, 1998).

Symptoms of acute pseudoephedrine exposure include increased blood pressure; increased, decreased or irregular heartbeat; shortness of breath, increased breathing rate, or troubled breathing; unusual nervousness, restlessness or excitement; and convulsions. The most common symptoms of pseudoephedrine overdose include mydriasis (dilated pupils), tachycardia (rapid heartbeat), hypertension (high blood pressure), hallucinations, arrhythmias (irregular heartbeat), agitation/anxiety, tremors/hyperreflexia, and vomiting (HSDB, 2002B). Acute exposure to pseudoephedrine hydrochloride may also cause nausea, constipation, dizziness, sedation, itching, anxiety, tenseness, weakness, paleness, difficulty in urination, insomnia, convulsions, central nervous system depression, and cardiovascular collapse with hypotension (low blood pressure) (Sigma, 2002A).

C. Chronic Effects

Tolerance to ephedrine may develop with prolonged or excessive use (USP, 1998).

Prolonged or repeated exposure to *d*- pseudoephedrine hydrochloride can cause hallucinations, central nervous system stimulation, psychic abnormalities such as anxiety, depression and excitability, and possibly coma (Acros, 2000B).

D. Skin Contact

I- Ephedrine hydrochloride may have a local anesthetic effect on exposed skin (Lewis, 2002).

E. Eye Contact

Ephedrine, when applied locally to the eye, may cause brow ache, headache, blurred vision, allergic conjunctivitis and dermatitis, irritation, and tearing (HSDB, 2002A).

F. Inhalation

Inhalation of dusts containing ephedrine or pseudoephedrine may cause respiratory tract irritation (Acros, 2000A; Acros, 2000C).

G. Ingestion

Ingestion is the most common route of exposure to ephedrine and pseudoephedrine. Information summarized in sections VI, A, B, and C (above), except where specifically noted, describe symptoms reported following ingestion of both drugs.

H. Predisposing Conditions

Ephedrine may induce anginal pain in persons with coronary insufficiency and/or ischemic heart disease. Ephedrine and pseudoephedrine are contraindicated in individuals with hypertension (high blood pressure), arteriosclerosis (thickening and hardening of the arterial walls), chronic heart disease, diabetes, cardiovascular disease, hyperthyroidism (increased thyroid functioning), prostatic hypertrophy (excessive growth of prostate gland), or a predisposition to glaucoma. Additionally, individuals sensitive to other sympathomimetics (e.g., albuterol, amphetamines, norepinephrine) and those receiving monoamine oxidase inhibitors (MAOI), myocardial-sensitizing anesthetics, or digitalis may be more susceptible to the adverse health effects of ephedrine and pseudoephedrine (HSDB, 2002A; USP, 1998; HSDB, 2002B).

I. Special Concerns for Children

Pseudoephedrine presents an increased risk of adverse effects for newborn and premature infants. Use of ephedrine and pseudoephedrine by nursing mothers is not recommended as pseudoephedrine passes into breast milk (HSDB, 2002A; USP, 1998).

VII. First Aid

The central nervous system effects of ephedrine may be mitigated by administration of a sedative or tranquilizer (HSDB, 2002A).

A. Eyes

Flush eyes immediately with water for at least fifteen minutes, occasionally lifting lower and upper lids, and obtain medical attention promptly (Acros, 2000A; Sigma, 1997; Acros, 2000B).

B. Skin

Exposed skin should be washed thoroughly with soap and water for at least fifteen minutes, and immediately remove contaminated clothing and shoes. Obtain medical assistance if irritation or rash appears (Acros, 2000A; Sigma, 1997; Acros, 2000B).

C. Ingestion

Do not induce vomiting. If conscious, rinse the mouth and drink 2-4 cups of milk or water. Never give anything by mouth to an unconscious person. Obtain medical aid (Acros, 2000A; Sigma, 1997; Acros, 2000B).

D. Inhalation

If inhaled, remove to uncontaminated area. Give artificial respiration if not breathing. If breathing is difficult, give oxygen. Obtain immediate medical attention (Acros, 2000A; Sigma, 1997; Acros, 2000B).

VIII. Standards for Inhalation Exposure

A. Occupational Exposure Limits (NIOSH, 1997; ACGIH, 1994)

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|--|------------------|
| 1. Ceiling Limit (C) (not to be exceeded at any time): | Not established. |
| 2. Short-Term Exposure Limit (STEL or ST): | Not established. |
| 3. 8-Hour Time Weighted Average (TWA): | Not established. |
| 4. 10-Hour Time Weighted Average (TWA): | Not established. |
| 5. Immediately Dangerous to Life & Health (IDLH): | Not established. |

Important Definitions Follow:

Ceiling Limit (C) is a concentration that must not be exceeded during any part of the workday.

Short-Term Exposure Limit (STEL or ST) is a 15-minute time-weighted average concentration that should not be exceeded during any part of the workday.

8-Hour Time Weighted Average (8-hour TWA) concentration is an exposure standard that must not be exceeded during any 8-hour work shift of a 40-hour workweek. 8-Hour TWA exposure standards established by the Occupational Safety and Health Administration (OSHA) are called Permissible Exposure Limits (PELs). 8-Hour TWA exposure standards established by the American Conference of Governmental Industrial Hygienists (ACGIH) are called Threshold Limit Values (TLVs).

10-Hour Time Weighted Average (10-hour TWA) concentration is an exposure standard that must not be exceeded during a 10-hour workday of a 40-hour workweek. 10-Hour TWA exposure standards developed by the National Institute for Occupational Safety and Health (NIOSH) are called Recommended Exposure Limits (RELs).

Immediately Dangerous to Life & Health (IDLH) defines a concentration which poses a threat of death or immediate or delayed permanent health effects, or is likely to prevent escape from such an environment in the event of failure of respiratory protection equipment. IDLH values are developed by the National Institute for Occupational Safety and Health (NIOSH).

“Skin” notation (NIOSH): significant uptake may occur as a result of skin contact. Therefore, appropriate personal protective clothing should be worn to prevent dermal exposure.

B. Emergency Response Planning Guidelines (1 hour or less) (AIHA, 2002)

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|--|------------------|
| 1. ERPG-1 (protective against mild, transient effects): | Not established. |
| 2. ERPG-2 (protective against serious adverse effects): | Not established. |
| 3. ERPG-3 (protective against life-threatening effects): | Not established. |

Emergency Response Planning Guidelines (ERPGs) are developed by the American Industrial Hygiene Association (AIHA) to assist in planning and preparation for catastrophic accidental chemical releases. ERPGs allow emergency response planners to estimate the consequences of large-scale chemical releases on human health, and evaluate the effectiveness of prevention strategies and response capabilities. ERPGs assume that the duration of exposure is one hour or less. They are not intended to be used as limits for routine operations and are not legally enforceable.

Definitions for the three ERPG levels are:

ERPG-1: an estimate of the maximum airborne concentration below which nearly all individuals could be exposed for up to one hour without experiencing more than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor.

ERPG-2: an estimate of the maximum airborne concentration below which nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair an individual's ability to take protective action.

ERPG-3: an estimate of the maximum airborne concentration below which nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.

C. Acute Reference Exposure Level (1-hour exposure) (OEHHA, 1999)

Level protective against mild adverse effects:

Not established.

D. Chronic Reference Exposure Level (multiple years) (OEHHA, 2002)

Level protective of adverse health effects:

Not established.

Reference Exposure Levels (RELs) are developed by the California EPA's Office of Environmental Health Hazard Assessment (OEHHA). A REL is a concentration at or below which no adverse health effects are anticipated, even in the most sensitive members of the general population (for example, persons with pre-existing respiratory disease). RELs incorporate uncertainty factors to account for information gaps and uncertainties in the toxicological data. Therefore, exceeding a REL does not necessarily indicate an adverse health impact will occur in an exposed population. Acute RELs are based on an assumption that the duration of exposure is one hour or less. Chronic RELs are intended to be protective for individuals exposed continuously over at least a significant fraction of a lifetime (defined as 12 years).

E. Chronic Reference Concentration (lifetime exposure) (IRIS, 2003)

Level protective of adverse health effects:

Not established.

IX. Environmental Contamination Concerns

A. Surface Water

No information available. Ephedrine and pseudoephedrine are not likely to result in significant surface water contamination unless very large quantities are spilled. The pH of a 1:200 aqueous solution is 10.8 (HSDB, 2002A; HSDB, 2002B).

B. Groundwater

No information available. Ephedrine and pseudoephedrine are not likely to result in significant groundwater contamination unless very large quantities are spilled. The pH of a 1:200 aqueous solution is 10.8 (HSDB, 2002A; HSDB, 2002B).

C. Drinking Water

Suggested No Adverse Response Level (NAS, 1980): Not established.

Preliminary Remediation Goal for Tap Water (U.S. EPA, 2002 Region IX): Not established.

D. Soil

No information available. Ephedrine and pseudoephedrine are not likely to result in significant soil contamination unless very large quantities are spilled. The pH of a 1:200 aqueous solution is 10.8 (HSDB, 2002A; HSDB, 2002B).

Preliminary Remediation Goal for Residential Soil (U.S. EPA, 2002 Region IX): Not established.

E. Air

No information available. Ephedrine and pseudoephedrine are not volatile. In powdered form, ephedrine and pseudoephedrine are potentially problematic indoors. Ephedrine and pseudoephedrine will be removed from the air by wet and dry deposition.

Preliminary Remediation Goal for Ambient Air (U.S. EPA, 2002 Region IX): Not established.

F. Indoor Surface Contamination

Ephedrine hydrochloride and pseudoephedrine hydrochloride are non-volatile salts and are relatively stable under typical indoor residential environmental conditions. Both compounds are reported to undergo gradual decomposition on exposure to light (HSDB, 2002A; HSDB, 2002B). Standards for cleanup of ephedrine and pseudoephedrine contamination on indoor surfaces have not been developed.

X. Personal Protective Equipment

Wear protective eyeglasses/chemical safety goggles, rubber boots, heavy rubber gloves, protective clothing, and a self-contained breathing apparatus. Launder contaminated clothing and shoes before reuse (Acros, 2000A; Acros, 2000B; Sigma, 1997).

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